

REMARKS

Claims 1-6, 10, 12, 15, 19, and 21 are pending. Due to a Restriction Requirement, claims 15 and 19 are withdrawn from consideration. Claims 1-6, 10, and 12 are objected to. Claims 1, 2, 4-6, 10, and 12 are rejected under 35 U.S.C. § 102, and claims 1-6, 10, 12, and 21 are rejected under 35 U.S.C. § 103. Applicants address each basis for objection and rejection as follows.

Claim Amendments

Claims 1-6, 10, 12, 15, and 19 have been amended to include an article at the beginning of the claim. In addition, claim 1 has been amended to recite that the expression system is for use in a producer cell line. Support for this amendment is found, for instance, in Example 1 of the application as filed.

No new matter has been added by the present amendments. Applicants reserve the right to pursue any cancelled subject matter in this or in a continuing application.

Objections to the Claims

Claims 1-6, 10, and 12 are objected to for lacking an article at the beginning of the claims. The claims have been amended to begin with an article. Applicants submit that this basis for objection may be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 1, 2, 4-6, 10, and 12 are rejected under 35 U.S.C. § 102(a) and 35 U.S.C. § 102(e) as being anticipated by Zheng et al. (U.S. Publication No. 2006/0057102; "Zheng"). The Office notes that Zheng has a publication date of March 16, 2006, a filing date of August 11, 2005, and a provisional priority date of *August 11, 2004*. The present application is the U.S. national stage of PCT/EP2005/003888 filed on April 13, 2005 and claims benefit of the filing date of EP 04008881.7, filed on *April 14, 2004*. The priority date of the present application precedes the August 11, 2004 priority date of Zheng. The Office notes that, while a certified copy of EP 04008881.7 has been submitted, the application is not in English. Applicants herewith provide a translation of EP 0400888.7 and a statement that the translation is accurate. The presently

claimed invention finds support throughout the EP 0400888.7 application (see, for example, page 3, lines 9-20 and page 14, line 10, to page 17, line 25, of the translation). Applicants submit that, in view of the submission of the translation of EP 0400888.7, the presently claimed invention is entitled to the benefit of the April 14, 2004 filing date of EP 0400888.7 and Zheng is not available as prior art under 35 U.S.C. § 102(a) or § 102(e). The anticipation rejection of claims 1, 2, 4-6, 10, and 12 over Zheng should be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1, 4, 6, 10, and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari-Lacraz et al. (J. Immunol. 167:3478-3485, 2001; “Ferrari-Lacraz”) in view of Sutherland et al. (Transplantation 69:1806-1812, 2000), and claims 2, 3, 5, and 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ferrari-Lacraz in view of Sutherland, and further in view of Kim et al. (U.S. Patent No. 7,279,568; “Kim”). Applicants address these bases for rejection, in turn, below.

Claims 1, 4, 6, 10, and 12

In asserting that claims 1, 4, 6, 10, and 12 are obvious, the Office, at page 7 of the Office Action, states that Ferrari-Lacraz “teaches that an IgG2a protein bearing the same Fc sequences as CTLA4/Fc and IL-15 mutant/Fcγ2a protein was used as a control” and that Sutherland “teaches cDNA encoding the murine CTLA4 was fused to IgG2c Fc (CTLA4Ig) and CD5 leader sequence was fused to the Fc of mouse IgG2c.” The Office further states (page 8):

One having ordinary skill in the art would have been motivated to combine the teachings of Ferrari-Lacraz et al. and the teachings of Sutherland et al. because Sutherland et al. teaches CD5 leader sequences can be fused to CTLA4/IgG2c Fc fusion for allograft purpose and a promoter to direct the expression of CTLA4/IgG2c Fc fusion protein.

Applicants respectfully traverse this basis for rejection.

Ferrari-Lacraz discloses an antagonistic IL-15/Fc fusion protein for use in a transplantation model, alone or in combination with CTLA4/Fc fusion protein. For this purpose, the IL-15/Fcγ2a fusion protein of Kim et al. (J. Immunol. 160:5742, 1998) was employed (see

Materials and Methods at the bottom of the left column at page 3479). This fusion protein was prepared using plasmids with an IgG kappa leader sequence. Sutherland discloses the transgenic expression of CTLA4/Fc (of IgG2c) fusion protein for use in a transplantation model. A CD5/IgG2cFc fusion was used as a negative control. Applicants disagree with the Office's assertion that Sutherland's Figure 3A teaches that a CD5 leader sequence can be fused to a CTLA4/IgG2v Fc fusion for the purpose of allografts. Sutherland uses the CD5 leader sequence fused to *Fc* (not a CTLA4/IgG2v Fc fusion) as a *negative control*. There is no disclosure or suggestion in Sutherland to use the CD5 leader sequence functionally linked to the nucleic acid sequence encoding the CTLA4/IgG2c Fc fusion, let alone the IL-15/Fc fusion.

Applicants submit that the combination of Ferrari-Lacraz with Sutherland fails to provide any suggestion or motivation to replace the IgG kappa leader sequence used by Ferrari-Lacraz with the CD5 leader sequence. In fact, Sutherland only uses the CD5 leader sequence as a *negative control*. Ferrari-Lacraz and Sutherland, even if combined, fail to describe or suggest any advantage for using the CD5 leader sequence over the IgG kappa leader sequence in expressing an IL-15/Fc fusion protein.

In contrast, Applicants have shown that, surprisingly, use of the CD5 leader sequence results in much higher expression of the IL-15/Fc fusion protein in a producer cell line than other leader sequences, including the IgG leader sequence (see, e.g., the paragraph spanning pages 22 and 23 of Applicants' specification published as WO 2005/100395 and Figure 8.) Use, in an expression system, of a CD5 leader sequence functionally linked to a nucleic acid sequence encoding an IL-15/Fc fusion protein is nonobvious over the cited art, which merely mentions use of a CD5 leader sequence in a control construct and not even a control construct expressing a fusion protein.

Applicants submit that the Office has used hindsight in combining the teachings of Ferrari-Lacraz and Sutherland to come to the claimed invention. The Office must identify a motivation to combine the references that create the case of obviousness. *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1457 (Fed. Cir. 1998). That is, "the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references

for combination in the manner claimed.” *Id.* (Emphasis added.) The Office, in this instance, has not met this requirement. Even if the Office identifies every element of a claimed invention in the prior art, this alone is insufficient to negate patentability. Otherwise, “rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. *Id.* The law requires more than conclusory statements, it requires evidence, and the Office has provided none.

Finally, Applicants note that claim 1 has been amended to clarify that the expression system is for use in a producer cell line, whereas Ferrari-Lacraz and Sutherland describe transplantation models. Applicants submit that one skilled in the art would recognize that designing an expression system for a producer cell line is subject to different considerations than designing a construct for transgenic expression for use in a transplantation model. Neither Ferrari-Lacraz nor Sutherland provides any guidance as to which leader sequences could be used for expression of an IL-15/Fc fusion protein in a producer cell line. For this reason as well, Applicants submit that the claims as amended are free of the obviousness rejection over Ferrari-Lacraz in combination with Sutherland.

Claims 2, 3, 5, and 21

The Office, at page 9, states that neither “Ferrari-Lacraz et al. (2001) nor Sutherland et al. (2000) explicitly teaches ‘a selectable marker gene’ recited in claim 5, and a CMV promoter with intron A being part of a transcription-regulating unit as recited in claims 2, 3, and 21.” The Office cites Kim as describing both a selectable marker gene and a CMV promoter with intron A being part of a transcription-regulating unit.

Claims 2, 3, 5, and 21 depend from claim 1. Applicants, as explained above, submit that claim 1 is nonobvious over the combination of Ferrari-Lacraz and Sutherland because the references, even if combined, fail to teach or suggest using a CD5 leader sequence functionally linked to a nucleic acid sequence encoding an IL-15/Fc fusion protein. Kim does not remedy this deficiency because it entirely fails to describe or suggest use of a CD5 leader sequence. This basis for the obviousness rejection may also be withdrawn.

CONCLUSION

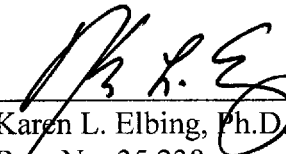
Applicants submit that the application is now in condition for allowance, and such action is hereby respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office Action for one (1) month, to and including March 12, 2010, and an authorization to charge the required extension fee to Deposit Account No. 03-2095.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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